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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/493,545	01/28/2000	Renwen Zhang	GI 5340A	2389

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EXAMINER
ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
1653	18

DATE MAILED: 06/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/493,545	Zhang et al.
Examiner	**Art Unit**
Hope Robinson	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 2, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 17
4) ☒ Interview Summary (PTO-413) Paper No(s). 18
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 4, 2002 has been entered.

Claim Disposition

2. Claims 1-21 are pending.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2, 4, 6, 7 and 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite for the recitation of "tissue source" as it is unclear what "tissue source applicant is referring to (see also claim 9). It is suggested that claim 2 for example, be combined with claim 15.

Claims 6, 7, 13 and 14 are indefinite for the recitation of "ligament-like tissue", as the metes and bounds of the claim are unclear. It is suggested that applicant rewrite the claim ot read "ligament".

Claim 7 is indefinite because the claim recites "**BMP-12, BMP-13 members of the BMP-12 subfamily and MP52. Note that a comma is missing, the claim should be amended to read "**BMP-12, BMP-13, members of the BMP-12 subfamily**..." (See also claim 14).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Hattersley et al. (U.S. Patent No. 5,700,774, December 23, 1997).

The claimed invention is directed to a method and composition for regeneration of articular cartilage comprising administering an effective amount of bone morphogenetic protein. The specification on page 2 states that claimed invention provides methods and compositions for treatment of patients who suffer from some form of articular cartilage injury or defect. Hattersley teach a method and composition for repairing, reducing or preventing damage to cartilage and cartilaginous tissue comprising administering BMP-2 and one or more additional proteins, for example, BMP-4, 5, 7, 12 and 13 together with PTHrP (see columns 1-2 of the reference and claims 1-4 of the present application). Hattersley also teach that BMP (BMP-1 to BMP 15) play an important role as regulators of bone and other tissue repair processes, and is involved in tissue formation, maintenance and repair. Further, Hattersley states that BMP-2 has been shown to be able to induce the formation of new cartilage and or bone tissue in vivo in animal models (see for example claims 2 and 9).

In addition, Hattersley teach that the methods of the claimed invention comprises proteins that have the ability to induce formation of other types such as tendon and ligament (see columns 3-4 of the reference and claims 6, 7, 13 and 14 of the present application). Hattersley teaches that a heterodimer such as VGR-2, MP52, MIS for example can be combined with BMP-2 and BMP-12 or 13 (see column 7 and claims 5, 7 of the present application. Therefore, the limitations of the present application are met by this reference.

5. Claims 1, 6-8, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Celeste et al. (U.S. Patent No. 5,658,882 August 19, 1997).

The claimed invention is directed to a method and composition for regeneration of articular cartilage comprising administering an effective amount of bone morphogenetic protein (see claim 1). Celeste teaches methods and compositions responsible for formation of cartilage, tendon, ligament and other tissues (see abstract and column 1). Celeste also teach the induction of tendon/ligament, would healing and other tissue repair using a composition comprising BMP-12, BMP-13 or MP-52 (see claims 6-8, 13 and 14). Therefore, the limitations of the claims are met by this reference.

6. It is noted that claims 1-14 were previously rejected under 35 U.S.C. 102(b) over Hattersley in Paper No. 5 and that the rejection was withdrawn in Paper No.7 by the previous examiner. However, note that the record isn't clear as to why this ground of rejection was withdrawn as applicant's arguments in Paper No. 6 was not persuasive. Applicant states that the cited reference provided a method using BMP-2 together with PTH for the regeneration of articular cartilage whereas the present invention is directed to BMPs in the regeneration of articular cartilage. Applicant's also state that the Hattersley reference does not teach or suggest the use of BMPs in conjunction with suitable tissue sources to improve healing such as osteochondral grafts. However, claims 15-21 which recite the use of osteochondral grafts were

newly submitted in Paper No. 6 and the rejection of record was over claims 1-14 which remains anticipated by Hattersley. The claimed invention is directed to a method which uses the open language of "comprising", therefore although, only BMP is recited in the claim a method that uses BMP and PTH reads on the claimed invention. As the reference still applies to the claimed invention the rejection under 35 U.S. C. 102(b) has been re-instituted. Note also that a reference is cited under 35 U.S.C. 102(b) that teaches the use of BMPs only, thus the claimed invention is anticipated by the prior art.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

8. Claims 1-21 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Hattersley et al. (U.S. Patent No. 5,700,774, December 23. 1997) in view of Nevo et al. (U.S. Patent No. 4,642,120, February 10, 1987).

The teachings of Hattersley are above as applied to claims 1-14. Hattersley does not explicitly teach the use of osteochrondral grafts. In-so-far-as Hattersley does not teach osteochrondral grafts, Nevo teach the use of osteochondral grafts in association with articular cartilage damage. Therefore, where Hattersley teach chondrocytes as a tissue source in cartilage development, it would have been obvious to one or ordinary skill in the art to have modified Hattersley by using the early teachings of Nevo to further support chondrocytes as a tissue source, as well as osteochondronal grafts. Therefore, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

9. Applicant's arguments filed on June 4, 2002 in Paper No. 16 have been fully considered but were not persuasive, thus, the rejection under 35 U.S.C. 103 remains. The response on page 2 contends that Hattersley teaches the use of BMP in combination with parathyroid hormone (PTH) and the claimed invention does not require PTH thus, the reference does not teach the

claimed invention. As stated in Paper No.18, the claimed method and composition does not exclude the use of a parathyroid hormone with the use of the open language "comprising". The claims are directed to a method comprising administering an effective amount of BMP and the method does not exclude other components that could be added to BMP. With regard to the Nevo reference applicant contends that one skilled in the art would not likely substitute PTH with osteochondral graft with the expectation of the regeneration of articular cartilage. This argument is also not persuasive as Hattersley teaches methods and compositions to regenerate cartilage comprising BMP-2 as well as BMP-4, 5, 7, 13 etc, see column 3 combined with PTH and compositions having any of the BMPs combined with a heterodimer, thus, it is evident from Hattersley that the key ingredient is the BMP. Further, Hattersley teaches that BMPs have been shown to be regulators of bone and other tissue repair processes and that BMP-2 can induce formation of new cartilage, therefore, it is evident that the combination of BMPs with other components are enhancers of the process as BMPs by themselves are effective in cartilage regeneration. Therefore, there is motivation to combine the teachings of the references, thus, the rejection remains.

Conclusion

10. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday- Friday from 9:00 A.M. to 5:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, can be reached at (703)308-2932.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS

Patent Examiner

Christopher S.F. Low

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